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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,942	12/05/2001	Robert J. Hariri	9516-100-999	7788

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,942	HARIRI, ROBERT J.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003* .

2a)☒ This action is **FINAL.** 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 25-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 25-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response submitted 9/8/03 has been entered. Claims 2-24 have been canceled. Claim 1 has been amended. Claims 25-46 are newly submitted.

Claim Objections

The prior objection is withdrawn because the objected claims are canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 7, and 10-24 under 35 U.S.C. 112, first paragraph is withdrawn because the claims and the subject matter recited in the claims have been canceled.

Claims 25-46 are newly rejected under 35U.S.C. 112 first paragraph, because the specification as originally filed does not describe the invention as now claimed. The original disclosure fails to support new claim recitation, "wherein said CD34+ stem cells are not obtained from cord blood" as now claimed. The phrase is now considered to be new matter.

MPEP 2163.06 notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT 'NEW MATTER' IS INVOLVED. APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE". MPEP 2163.02 also teaches that "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN THAT APPLICATION". In the instant case, the specification as originally filed defines that "cord blood" is the umbilical cord blood (Specification, page 2, line 6), and that conventional technique for collecting cord blood is usually placing needle or cannula in the umbilical vein and gently massaging the placenta to aid in draining the cord blood. The specification also teaches that the placenta is a known source of hemopoietic pluripotent progenitor stem cells. The specification goes on to teach, "*it is a primary object of the present invention to provide a method of extracting and recovering hematopoietic stem cells from an exasaguinated placenta. It is also an object of the invention to provide a method for isolating other embryonic-like and/or omnipotent stem cells from an extractant of a drained placenta. It is a further object of the invention to provide a method to collect stem cells from the umbilical cord vein*" (Specification, page 2, last three paragraph, emphasis added). Applicant indicated that pages 2-5 support claim

25, however, as analyzed above, the specification does not appear to support the new claim. Accordingly, considering the teachings as a whole, it is clear that collecting stem cells from a mammalian placenta encompasses collection of cord blood via umbilical vein as now claimed in claim 28. Moreover, the specification is silent with regard to obtaining CD34+ stem cells from a source other than cord blood. Therefore, new claims 25 and 28 are not only conflicting with each other and with the teaching of the specification, but also introduced new matter to the specification because they represent a departure from, or addition to the disclosure of the application as filed.

For reasons set forth above, the amendment filed 9/8/03 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention.

Applicant is required to cancel the new matter in the reply to this Office Action.

To the extent that the claimed methods are not described in the instant disclosure, claims 25-46 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. Especially, the specification is silent with regard to how to collect placenta stem

cells not via umbilical vein and artery. The skilled in the art could not practice the invention without first carrying out undue experimentation as now claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 25-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 25-46 are vague and indefinite because the specification is unclear with respect to the definition of "placental stem cells" and "embryonic-like stem cells". In response to the previous rejection over the term "embryonic-like stem cells", applicants indicated that claims have been amended to recite "placental stem cell". Accordingly, the Examiner can only assume that a placental cell equals the embryonic-like stem cells (even though the specification fails to teach the two terms are equivalent). As an initial matter, the specification again fails to specifically define the term "placental stem cells". In the first action on merit, for the interest of compact prosecution and in light of the specification, the Examiner indicated that the term would be interpreted as encompassing "hematopoietic stem cells". In the 9/8/03 response, the applicant alleges that the assumption is flawed, and states, "embryonic-like stem cells are derived from the placenta". Interestingly, the specification teaches that the placenta is a known source of hematopoietic stem cells (Specification, page 2, lines 6-7), thus, stem cells derived from the placenta appear to include hematopoietic stem cells.

Additionally, new claims 25-46 are drawn to collecting CD34+ stem cells from an isolated mammalian placenta, and it is a well known that majority of hematopoietic stem cells are CD34+. Thus, the Examiner's assumption still stands. Moreover, the definition as indicated describes *where* the cells are obtained but is insufficient to define *what* the cells are because a mammalian placenta contains many different cell types. For example, the specification teaches that the placenta could be used to collect hematopoietic stem cells, other embryonic-like and omnipotent stem cells (Specification, page 2), and mensenchymal stem cells (Specification, page 12, 1st paragraph). In view of the purposed definition for embryonic-like or placenta stem cells, the counsel's arguments, and the teaching of the specification, it is unclear which of the stem cells are encompassed or excluded from the placental stem cells, thus, the metes and bounds of the claims are unclear.

Secondly, it appears that the applicant intends to exclude the hematopoietic stem cells from the placental stem cells because the applicant alleges that the Examiner wrongly assumed that the "embryonic-like stem cells" include hematopoietic stem cells, and states "embryonic-like stem cells are derived from the placenta". As discussed above, the specification teaches that the placenta is a known source of hematopoietic stem cells (Specification, page 2, lines 6-7), thus, stem cells derived from the placenta appear to include hematopoietic stem cells. Apparently, the arguments contradict the teaching of the specification. The arguments also contradict the common knowledge in the art. For example, Medline database defines stem cells collected from fetal blood

to include hematopoietic stem cells, and are from blood remaining in the umbilical cord and placenta (Mesh Term database). Here, the cord blood and placenta blood are considered as a whole, they are not considered as separate entities. To this end, the specification does discuss "isolation of placental stem cells" in the section bridging pages 11 and 12, wherein the only type of stem cells disclosed is "MSC", presumably, mesenchymal stem cells. As indicated in the specification and in the 9/8/03 response, embryonic-like stem cells (now placental stem cells) are derived from the placenta". In light of such definition and for the sake of a compact prosecution, the now recited "placental stem cells" would be considered as any stem cell derived from a mammalian placenta, which would contain HSC and MSC.

It is noted that mesenchymal stem cells are CD34- as taught by *Minguell et al* (Exp Biol Med 2001;226:507-20), thus, claim 25 and dependent claims appear to exclude collecting MSCs.

Claims 26, 27, 32, and 36-39 recite the limitation "said placenta stem cells". There is insufficient antecedent basis for this limitation in the claim, because the claims depend from claim 25, which does not recite "a placenta stem cell".

Claim 26 recites the limitation "said residual cells". There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

Claim 28 is objected to for failing to further limit a base claim because claim 25 requires perfusing placenta to collect CD34+ stem cells from a placenta but not cord blood, and claim 28 requires perfusing placenta via umbilical vein and artery, which is the means of collecting core blood as taught in the specification (page 2, 2nd paragraph). Thus, in light of the teaching of the specification, claim 28 fails to further limit the base claim.

Claims 35-39, 41, and 42 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 stands rejected and claims 26-46 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Boyse et al* (US 6,461,645), in view of *Belvedere et al* (Stem Cells 2000 July;18:245-51), *Sanders* (US 3,862,002), and *Addison et al* (J Steroid Biochem Mole Biol 1991;83-90).

In 9/8/03 response, Applicant argues that the references were combined pursuant to a flawed assumption that embryonic like stem cells includes

hematopoietic stem cells, and states that this is not the case, and "embryonic-like stem cells are derived from the placenta".

In response, as discussed in § 112, 2nd paragraph, the specification teaches that the placenta is a known source of hematopoietic stem cells (Specification, page 2, lines 6-7), thus, cells derived from the placenta would include hematopoietic stem cells. Therefore, the Boyse and Belvedere references still apply. Moreover, the combined references teach a method that would have the same method steps as presently claimed, thus, in addition to HSCs, the stem cells obtained would contain other placental stem cells, such as MSCs.

Applicant goes on to argue that using perfusion as means of obtaining stem cells was not taught by Sander and Addison.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, both Boyse and Belvedere teach obtaining stem cells from placenta. In addition to HSC, Boyse et al also teach that all the known progenitor cells are present in cord blood in high numbers (column 12, lines 24-26), that HSC has been found in a much higher level in the placenta than in the adult [peripheral blood], and that human fetal and cord blood has been shown to contain megakaryocyte and burst erythroblast progenitors. *Belvedere et al* teach maximizing the collection of stem cells from the placenta

using an apparatus comprising continued collection of blood flow using a device following common UCB collection procedures. They teach the same concern as taught in the specification, i.e. the yield is very low from the usual drainage of the umbilical vein. *Belvedere et al* reviewed commonly used drainage method including open and closed drainage systems and it is noted that *Belvedere et al* concerns the cost/efficiency factor for obtaining stem cells in a clinical setting (left column, page 246). *Sanders* and *Addison et al* teach the closed drainage system that perfuse placenta in a continued mode via umbilical vein and artery pair. The references are relied upon as a showing that the perfusion via umbilical vein and artery is known in the art as a closed system and continued mode of collecting biological materials from the placenta.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Boyse et al*, *Belvedere et al*, *Sanders*, and *Addison et al*, by combining or substituting the pressure device with the perfusion in collecting placenta stem cells with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because it is known that the additional blood from placenta after common procedure not only increased the volume of the collected blood but also increased the quantity of stem cells as taught by *Belvedere et al*. It should also noted although it is a well-known fact that it is desirable and feasible to maximize the HSC collection by a continuous mode of collection, often times, the cost/efficiency factor takes priority in a clinical setting,

thus even though it is obvious that using perfusion would maximize the stem cell collection, perfusion has not been widely used possibly for the cost concern.

New claims add new limitations such as the volume of the perfusion solution, specific anticoagulants, and supplementing cytokines and growth factors in the perfusion solution, which are well known knowledge in the art and taught by the cited references. For example, *Belvedere et al* teach that the volume range for collected cord blood is 20-200 ml (right column, page 245). Boyse et al teach that anticoagulants are heparin, EDTA, and CPDA (column 11, lines 27-41), and supplementing growth factors and cytokines to the obtained stem cells for desired biological function (column 20, § 5.1.3.2). Given the knowledge of the skill, these limitations fall within bounds of optimization. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The prior rejection of claims 1-6, 8, 9, and 11 under 35 U.S.C. 103(a) as being unpatentable over *Boyse et al* (US 6,461,645), *Belvedere et al* (Stem Cells 2000 July;18:245-51), *Sanders* (US 3,862,002), and *Addison et al* (J Steroid Biochem Mole Biol 1991;83-90), as applied to claims 1-6, 8, 11 above, and further in view of *Bersinger et al* (Reprod Fertil Dev 1992;4:585-8), is withdrawn because claim 9 has been canceled.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 stands provisional rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16 and 17 of copending Application No. 10/074,976.

Applicants request the Office hold this rejection in abeyance until such time as relevant claims of the '976 application or the instant application is allowed.

The prior provisional rejection of claims 1, 6, and 8 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-33 of copending Application No. 10/076,180, is withdrawn in view of the restriction practice in the cited application.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942 (571-272-0730, after the Office relocation in January, 2004). The examiner can normally be reached on 9:30 am - 6 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Q. Janice Li
Patent Examiner
Art Unit 1632

QJL
November 24, 2003

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER